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Squamous Cell Carcinoma of the Vulva in the South of Israel: A Study of 50 Cases

BENJAMIN PIURA, MD, FRCOG,[1]* ALEX RABINOVICH, MD[1] YORAM COHEN, MD,[2] MICHAEL FRIGER, PhD,[3] AND MAREK GLEZERMAN, MD[1]

[1]*Unit of Gynecologic Oncology, Department of Obstetrics and Gynecology, Soroka Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel*

[2]*Institute of Oncology, Soroka Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel*

[3]*Department of Epidemiology, Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel*

Background and Objectives: Vulvar carcinoma accounts for 4.9% of all female genital tract malignancies in the south of Israel. The most common histologic type is squamous cell carcinoma (82%). The purpose of this study was to investigate the clinical findings, treatment, and outcome of patients with vulvar squamous cell carcinoma in the south of Israel.

Methods: Data from the files of 50 patients with vulvar squamous cell carcinoma who were managed at the Soroka Medical Center between January 1961 and December 1996 were evaluated.

Results: Mean age at diagnosis was 67.1 years. The most prevailing presenting symptoms were vulvar lump, ulcer, and itching. Mean patient delay in seeking medical help was 48.2 months. Clinical palpation as a test for detecting groin lymph node metastases had a sensitivity and specificity of 57.1% and 61.5%, respectively. The 5-year survival rate was 60.3% overall. By means of univariate analysis, a significant worsening in survival was demonstrated with advancing stage of disease ($P < 0.001$), tumor >4 cm ($P < 0.001$), and positivity of surgical margins ($P < 0.0001$). In a multivariate analysis (Cox proportional hazards model) in a group of 45 patients, stage of disease was the strongest and the only significant predictor of survival ($P = 0.0098$).

Conclusions: Vulvar squamous cell carcinoma predominantly affects older women. Stage of disease, tumor size, and status of surgical margins are sensitive predictors of survival. The treatment of choice for most patients is surgery consisting of radical vulvectomy and bilateral groin lymphadenectomy.

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KEY WORDS: **radical vulvectomy; groin lymph nodes; surgical margins; vulvar lump; staging; survival**

INTRODUCTION

Cancer of the vulva is an uncommon malignancy accounting for only 0.3% of all cancers in women and 3–5% of all female genital tract malignancies, with an estimated incidence of 1–2/100,000 women [1–3]. The predominant histologic type is squamous cell carcinoma, which accounts for ~80–85% of the cases, followed by malignant melanoma (5%), basal cell carcinoma (2.5%), Paget's disease (2.5%), Bartholin's gland carcinoma (2%), and other rare histologic types [2,4]. Because of its

*Correspondence to: Benjamin Piura, MD, Unit of Gynecologic Oncology, Department of Obstetrics and Gynecology, Soroka Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, P.O. Box 151, Beer-Sheva 84101, Israel. Fax No.: (972)7-640-3503. E-mail: piura@bgumail.bgu.ac.il

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relative rarity, only a few centers in the world have gained experience with large series of this disease.

The Soroka Medical Center (SMC) in Beer-Sheva is the only tertiary care medical facility in the south of Israel that provides hospital care for a population of ~500,000: Jews from various ethnic origins make up ~80% of the population and Arab-Bedouins account for the remaining 20%. From the inauguration of the SMC in January 1961 until December 1996, 1,233 malignancies of the female genital tract were diagnosed: 387 (31.4%) uterine corpus cancers, 380 (30.8%) ovarian cancers, 368 (29.8%) uterine cervix cancers, 61 (4.9%) vulvar cancers, 12 (1.0%) fallopian tube cancers, six (0.5%) placental cancers, five (0,4%) vaginal cancers, and 14 (1.1%) cancers of unspecified site. Of the 61 vulvar cancers, 50 (82%) were squamous cell carcinoma, four (6.5%) were malignant melanoma, four (6.5%) were basal cell carcinoma, and three (4.9%) were Paget's disease of the vulva. The aim of the present study was to report the clinical findings, treatment, and outcome of the 50 patients with vulvar squamous cell carcinoma.

MATERIAL AND METHODS

The clinical and pathological records of 50 patients with squamous cell carcinoma of the vulva who were managed at the Soroka Medical Center, Beer-Sheva, Israel, between January 1961 and December 1996 were reviewed. When warranted, surgery consisted of either radical vulvectomy and bilateral groin lymphadenectomy with use of the en-bloc butterfly incision technique, or radical vulvectomy and bilateral groin lymphadenectomy with use of the three-separate incision technique, or radical vulvectomy and unilateral groin lymphadenectomy, or radical vulvectomy without groin lymphadenectomy, or simple vulvectomy or wide local excision. The groin lymph node dissection consisted of removal of all superficial and deep lymphatic fatty tissue around the femoral artery, femoral vein, and great saphenous vein in the femoral triangle. For patients who received radiotherapy to the whole pelvis and/or vulva, it consisted of external megavoltage photonic irradiation employing a 10 MeV linear accelerator delivering 4,500–5,040 cGy in daily fractions of 180 cGy. For patients who received chemotherapy, it consisted of cisplatin 75 mg/sqm (day 1) and 5-fluorouracil (5-FU) 750 mg/sqm (days 2–5).

The following data were retrieved from the files of the patients: ethnic origin, age at diagnosis, pre- or postmenopausal status, age at menarche, age at menopause, parity, family status, associated diseases, body weight, presenting symptoms, time interval from the beginning of symptoms until diagnosis of vulvar malignancy, tumor size and site on the vulva, stage of disease, result of clinical assessment of groin lymph nodes, method of treatment, type of surgery, result of histopathologic examination of groin lymph nodes, status of surgical margins, postoperative complications, time interval from initial diagnosis until detection of recurrence, site of recurrence, method of therapy for recurrent disease, and results of follow-up. Twenty-six patients in whom initial surgery had included groin lymph node dissection were retrospectively staged according to the recently revised International Federation of Gynecology and Obstetrics (FIGO) staging system for vulvar carcinoma, which includes histopathological examination of groin lymph nodes [5], after thorough record review. Patients in whom initial surgery had not included groin dissection were staged according to the old (clinical) FIGO staging system for vulvar carcinoma with the exeption that perineal involvement per se, as in the revised FIGO staging system, did not allocate a higher stage than Stage I or II. Recurrent disease was documented in patients in whom histopathological examination of the primary surgical specimen demonstrated tumor-free margins and who were free of disease after initial surgery and then developed clinical and histopathological evidence of squamous cell carcinoma in one or more of the following sites: vulva, groin, pelvis, and distant organs.

The material was analyzed with regard to stage of disease (Stages I+II combined vs. Stages III+IVA+IVB combined), tumor size (<4 cm vs. >4 cm), ethnic origin (Ashkenazi vs. Sephardic), age (<60 vs. >60), tumor grade (Grade 1 vs. Grades 2 and 3 combined), tumor site (clitoris vs. other than clitoris), clinical assessment and histopathologic examination of groin lymph nodes (negative nodes vs. positive nodes), status of surgical margins (tumor-free versus involved), recurrence-free interval (<2 years vs. >2 years), follow-up status, and survival rate. Survival was calculated using the Kaplan-Meier method [6] and compared satatistically with use of the log-rank test [7]. The Cox proportional hazards model [8,9] was employed in order to evaluate the joint effects of various clinical variables on survival.

RESULTS

All 50 patients were Jewish. Twenty (40%) were of European-American origin (Ashkenazi) and 30 (60%) were of Asian-African origin (Sephardic). Age at diagnosis was recorded in 49 patients and ranged from 33–87 years (mean, 67.1 years). The distribution of patients according to age group is displayed in Table I. Of the 50 patients, one (2%) was premenopausal and 49 (98%) were postmenopausal. Age at the menarche ranged from 11–18 years (mean, 13.9 years). Age at the menopause ranged from 32–60 years (mean, 48.1 years). Parity was recorded in 49 patients: five (10.2%) were nulliparous and 44 (89.8%) had at least one child at the time of diagnosis. The mean parity of the parous patients was 5.54 (range, 1–16 children). Family status at the time of diagnosis was recorded in 49 patients: 24 (49%) were married, 23 (46.9%) were widows, and two (4.1%) were

TABLE I. Distribution of Patients With Vulvar Squamous Cell Carcinoma According to Age Group (n = 49)

Age (years)	No. of patients	%
30–39.9	1	2.0
40–49.9	1	2.0
50–59.9	9	18.4
60–69.9	19	38.8
70–79.9	13	26.5
80–89.9	6	12.2

TABLE II. Presenting Symptoms of Vulvar Squamous Cell Carcinoma (n = 45)

Symptom[a]	No. of patients	%
Lump	31	68.9
Pruritus	25	55.6
Ulcer	19	42.2
Bleeding	11	24.4

[a]Some patients presented with a combination of symptoms; therefore percentage adds up to >100%.

TABLE III. Distribution of Patients With Vulvar Squamous Cell Carcinoma According to Tumor Site (n = 47)

Site	No. of patients	%
Left side of vulva without involvement of the clitoris and/or fourchette	20	42.6
Right side of vulva without involvement of the clitoris and/or fourchette	16	34.0
Clitoris alone or clitoris with involvement of other sites	10	21.3
Fourchette alone	1	2.1

single. Data with respect to blood pressure and diabetes mellitus were available in 46 patients: 15 (32.6%) were hypertensive (blood pressure >140/90) and 15 (32.6%) were diabetic. Information about cigarette smoking was available in 41 patients: only one patient (2.4%) was a smoker. Body weight at the time of diagnosis was recorded in 45 patients: nine (20%) were obese (>25 kg above ideal body weight) and 36 (80%) were not obese. Of the 50 patients, one (2%) had a second primary malignancy occuring synchronously with vulvar carcinoma (non-Hodgkin's lymphoma).

Presenting symptoms were recorded in 45 patients and are detailed in Table II. The most prevailing presenting symptoms were vulvar lump, ulcer, and itching. The time interval from the beginning of symptoms until seeking medical attention was recorded in 39 patients and ranged from 1 week to 41 years (mean, 48.2 months). Tumor diameter at the time of diagnosis was recorded in 45 patients and ranged from 0.5–15 cm (mean, 3.8 cm). Tumor site was recorded in 47 patients (Table III).

Twenty patients (40%) had Stage I, 11 (22%) had Stage II, 13 (26%) had Stage III, 3 (6%) had Stage IVA, and 3 (6%) had Stage IVB. Thirty-eight (76%) had a well-differentiated (G1) tumor, 7 (14%) had a moderately well differentiated (G2) tumor, 2 (4%) had a poorly differentiated (G3) tumor, and in three (6%) the differentiation of the tumor was not recorded.

The distribution of treatment modalities in relation to FIGO staging is displayed in Table IV. Forty-two patients (84%) underwent surgery and eight (16%) did not. Of the 12 patients (24%) who had radiotherapy, nine had postoperative adjuvant external pelvic radiotherapy because of positive groin lymph nodes at initial surgery, and three had radiotherapy to the vulva as primary treatment. One patient received chemotherapy alone (cisplatin and 5-fluorouracil) and four patients had no treatment. The distribution of patients who had surgery according to type of surgery is shown in Table V.

Data with respect to groin lymph node metastases were available in 21 of the 26 patients who had radical vulvectomy and groin lymph node dissection. Of these patients, 13 (61.9%) had histologically positive nodes and eight (38.1%) had histologically negative nodes. Data with respect to both clinical palpation and histopathologic examination of groin lymph nodes were available in 20 of the 26 patients who had radical vulvectomy and groin lymph node dissection (Table VI). Clinical palpation detected palpable nodes (clinically positive nodes) in nine patients and failed to detect palpable nodes (clinically negative nodes) in 11 patients. Of the nine patients who had clinically positive nodes, histopathologic examination detected positive nodes (true positive) in four patients and negative nodes (false positive) in five patients (predictive value positive of clinical palpation, 44.4%). Of the 11 patients who had clinically negative nodes, histopathologic examination detected positive nodes (false negative) in three patients and negative nodes (true negative) in eight patients (predictive value negative of clinical palpation, 72.7%). Overall, of the 20 patients in whom data with respect to both clinical palpation and histopathologic examination of groin lymph nodes were available, histopathologic examination detected positive nodes in seven patients and negative nodes in 13 patients. The sensitivity (detection rate) and specificity of clinical palpation as a test for detecting groin lymph node metastases were 57.1% and 61.5%, respectively.

Information about margins of the surgical specimen was available in 37 patients: 30 (81.1%) had tumor-free surgical margins and seven (18.9%) had involved surgical margins.

Of the 30 patients who had radical vulvectomy, 16 (53.3%) had postoperative complications. The most prevailing postoperative complications were wound dehiscence and leg lymphedema. (Table VII).

TABLE IV. Treatment Modalities in Relation to FIGO Staging of Patients With Vulvar Squamous Cell Carcinoma (n = 50)*

Stage	Surgery alone	Surgery & RT	RT alone	Chemo alone	No treatment	Total (%)
I	18	2	—	—	—	20 (40.0%)
II	10	1	—	—	—	11 (22.0%)
III	5	4	2	—	2	13 (26.0%)
IVA	—	1	1	—	1	3 (6.0%)
IVB	—	1	—	1	1	3 (6.0%)
Total	33	9	3	1	4	50 (100.0%)
(%)	(66.0%)	(18.0%)	(6.0%)	(2.0%)	(8.0%)	(100.0%)

*RT, radiotherapy; Chemo, chemotherapy.

TABLE V. Distribution of Patients According to Type of Surgery (n = 42)*

Type of surgery	No. of patients	%
RVND with use of the butterfly incision technique	21	50
RVND with use of the 3-separate incision technique	3	7.1
RV with unilateral groin lymph node dissection	2	4.8
RV without groin lymph node dissection	4	9.5
Simple vulvectomy	3	7.1
Wide local excision	9	21.4
Total	42	100.0

*RV, radical vulvectomy; RVND, radical vulvectomy and bilateral groin lymph node dissection.

TABLE VI. Clinical Palpation in Relation to Histopathologic Examination of Groin Lymph Nodes in Vulvar Squamous Cell Carcinoma (n = 20)*

Clinical palpation	Histopathologic examination		Total
	Positive	Negative	
Positive	4 (TP)	5 (FP)	9
Negative	3 (FN)	8 (TN)	11
Total	7	13	20

*Sensitivity (TP/TP + FN) = 57.1%; Specificity (TN/TN + FP) = 61.5%; Predictive value positive (TP/TP + FP) = 44.4%; Predictive value negative (TN/TN + FN) = 72.2%. TP, True positive; FP, False positive; TN, True negative; FN, False negative.

Of the 48 patients in whom data with respect to recurrence was available, 13 (27,1%) developed recurrent disease (6 patients originally had Stage I, 3 had Stage II, and 4 had Stage III disease). The mean recurrence-free interval was 31.5 months. The vulva was affected by recurrence in 11 patients, the pelvis in one patient, and the liver in one patient. Method of therapy for recurrent disease included surgery alone (9 patients), radiotherapy alone (3 patients), and combination of radiotherapy and chemotherapy (1 patient).

Follow-up ranged from 1–326 months, with 37 (74%) of the 50 patients followed for at least 5 years or until time of death. Nineteen patients (38%) were alive free of disease, 18 (36%) had died of disease, and 13 (26%) had

TABLE VII. Complications After Radical Vulvectomy for Vulvar Squamous Cell Carcinoma (n = 30)

Type of complication[a]	No. of patients	%
Wound dehiscence	8	26.7
Leg lymphedema	8	26.7
Leg lymphangitis	2	6.7
Groin lymphocyst	1	3.3
Urinary problems	1	3.3
No complications	14	46.7

[a]Some patients had more than one complication; therefore percentage adds up to >100%.

died of intercurrent disease. The actuarial 5-year survival rate was 60.3% overall; 78.2% for Stage I, 83.3% for Stage II, 38.4% for Stage III, 33.3% for Stage IVA, and 0% for Stage IVB; 79.3% for Stages I+II combined and 32.9% for Stages III+IVA+IVB combined; 60.2% for Grade 1, 50% for Grade 2, and 100% for Grade 3; 88.4% for patients who had tumor-free surgical margins and 0% for patients who had involved surgical margins; 70.1% for tumor size <4 cm and 29.9% for tumor size >4 cm; 85.7% for patients who had radical vulvectomy, 70.1% for patients who had simple vulvectomy or wide local excision, and 0% for patients who had no surgery; 62.2% for patients with histopathologic positive groin lymph nodes and 56.3% for patients with histopathologic negative groin lymph nodes; 73,3% for Ashkenazi patients and 52.1% for Sephardic patients; 76.2% for patients <60 years and 54.9% for patients >60 years; 42% for tumors involving the clitoris and 61.4% for tumors not involving the clitoris; 66.7% for patients who developed a recurrence >2 years after initial treatment and 28.6% for patients who developed a recurrence <2 years after initial treatment. Univariate analysis with use of the log-rank test of the following variables: stage of disease, tumor size, ethnic origin, age of the patient, tumor grade, tumor site on the vulva, and recurrence-free interval demonstrated that only each of the following variables: stage of disease ($P < 0.001$) and tumor size ($P < 0.001$) was a significant predictor of survival. In patients who had surgery, univariate analysis of the following additional variables: status of surgical margins and lymph node status, revealed that status of surgical margins ($P < 0.0001$) was

TABLE VIII. Multivariate Analysis (Cox Proportional Hazards Model) of Clinical Variables With Endpoint Dead in Vulvar Squamous Cell Carcinoma (n = 45)

Variable	Relative hazard	95% Confidence interval	*P* value
Stage			
I+II	1.000	Reference	
III+IVA+IVB	7.898	1.647–37.871	0.0098
Tumor site			
Other than clitoris	1.000	Reference	
Clitoris	2.876	0.698–11.842	0.1433
Tumor size			
<4 cm	1.000	Reference	
>4 cm	2.304	0.706–7.522	0.1665
Ethnic origin			
Ashkenazi	1.000	Reference	
Sephardic	2.030	0.555–7.426	0.2844
Age			
<60 years	1.000	Reference	
>60 years	0.832	0.212–3.268	0.7392

also a significant predictor of survival, whereas lymph node status was not. Multivariate analysis with use of the Cox proportional hazards model was employed for 45 patients in order to evaluate the joint effects of stage of disease, tumor site, tumor size, ethnic origin, and age on survival. It demonstrated that only stage of disease ($P = 0.0098$) was a significant predictor of survival (Table VIII). However, when multivariate analysis with use of the Cox proportional hazards model was employed for 34 patients who had surgery in order to evaluate the joint effects of stage, ethnic origin, tumor site, age, tumor grade, and status of surgical margins on survival, status of surgical margins turned out to be a significant predictor of survival ($P = 0.0032$), whereas ethnic origin was of borderline significance ($P = 0.0484$).

DISCUSSION

Vulvar carcinoma is the fourth most common female genital tract malignancy in the south of Israel, ranking after ovarian, uterine corpus, and uterine cervix cancer, and accounting for 4.9% of all female genital tract malignancies. The incidence has been estimated to be 1–2 per 100,000 women, or approximately one-third that of cervical carcinoma in Israel [10,11]. Although Arab-Bedouins make up ~20% of the population in the south of Israel, not even a single case of vulvar carcinoma was encountered among Arab-Bedouin women during the entire 36 years of the study period. This is in accord with other studies that demonstrated a very low incidence rate of vulvar carcinoma in strict Muslim women, whose pubes are shaved and whose vaginal toilet is extremely scrupulous [12]. In contrast to cancer of the uterine cervix, there is no evidence that the incidence of vulvar carcinoma in Jewish women is lower than in non-Jewish women [13]. The ratio of Jewish women of Asian-African origin (Sephardic) to Jewish women of European-American origin (Ashkenazi) affected by vulvar carcinoma in this series (3:2) is similar to that of Sephardic to Ashkenazi Jews in the general population of the south of Israel. We, however, have noticed a poorer outcome in Sephardic women (5-year survival, 52.1%) as compared to Ashkenazi women (5-year survival, 73.3%), but on a univariate analysis the difference was not statistically significant ($P > 0.05$). However, on a multivariate analysis in a group of 34 patients who had surgery, it turned out to be of borderline significance ($P = 0.0484$). The trend for a poorer outcome in Sephardic women as compared to Ashkenazi women may be explained by the lower socioeconomic status of the Sephardic population in the south of Israel, a factor that most probably had contributed to patient delay in seeking medical assistance.

In this series, the most common age group of patients with vulvar carcinoma was 60–69.9 years (38.8% of the patients), and although the age range extended from the third to the ninth decade of life, only 4% of the patients were <50 years of age and only 2% of the patients were premenopausal. This finding corroborates previous studies that demonstrated that the most common age group of patients with vulvar carcinoma is 60–69.9 years [12,14]. In Rothschild's series of 331 patients (published in 1912) [14], the percentage of patients >70 was 12%, whereas in Way's series of 642 patients (published in 1982) [12], the percentage of patients >70 was 28.4%. This increase over the years in the proportion of elderly patients affected by vulvar carcinoma is presumably a reflection of increased longevity at latest years [3]. We have noticed a trend for a poorer survival in patients over the age of 60 (5-year survival, 54.9%) as compared to patients <60 years of age (5-year survival, 76.2%), but the difference was not statistically significant ($P > 0.05$).

Since vulvar carcinoma occurs in older women, it is not surprising that we, and others [12], have found that a high percentage (36–47%) of them are widows. In contrast to Way's series [12] in which 20% of the patients were single, in this series only 4.1% of the patients were single. In contradistinction to carcinoma of the uterine cervix, sexuality does not seem to play an important part in the etiology of vulvar carcinoma. In contrast to Way's series [12] in which 23% of the patients were nulliparous, in this series only 10.2% of the patients were nulliparous. There does not appear to be any significant association between vulvar carcinoma and parity [2]. Menstrual histories (menarche and menopause) of patients with vulvar carcinoma do not seem to be different from menstrual histories of women in the local general population. We have found that almost one-third of the patients with vulvar carcinoma were hypertensive and/or diabetic and one-fifth were obese. However, high blood pressure, ab-

normal carbohydrate intolerance, and obesity are prevalent in the elderly population and do not appear to be significant risk factors of vulvar carcinoma by themselves [2,3].

The most common presenting symptoms of vulvar carcinoma are vulvar mass, ulcer, and itching, and biopsy of the vulvar lesion is mandatory in making the diagnosis of this disease. In contradistinction to Way's series [12], in which bleeding was a very rare symptom (1.4% of the patients), bleeding was encountered in almost one-quarter of the patients in this series.

Most distressing are the data concerning patient dalay in seeking medical help. This attitude of the patients is, most probably, due to false modesty and fear. In this series, the mean duration of patient delay was 4 years, but there were patients who had seeked medical assistance >10 years after the beginning of symptoms. It has been a universal experience that patients with vulvar cancer tend to be very slow to seek medical assistance [2,12]. Cavanagh et al. [15] reported a patient delay of >12 months in 99 of 296 patients (33%). Rutledge et al. [16] reported that 60% of their patients were aware of a vulvar mass or sore for an average period of 10 months before treatment. Sometimes, delay may be caused by the patient's family doctor who fails to diagnose the disease because of failure to examine the patient, and sometimes even surgeons on referral may miss the diagnosis because of failure to perform a biopsy [12]. Rutledge et al. [16] reported that in 30% of their patients, there was a physician delay of 3 months or more, and 25% had been under medical treatment without having a biopsy.

In this series, the clitoris was involved in about one-fifth of the patients. The outcome of the patients in whom the clitoris was involved was worse than that of the patients in whom the clitoris was not involved, but the difference was not statistically significant. The poorer outcome in the presence of clitorial involvement may be explained by the alternative direct lymphatic drainage from the clitoris to the pelvic obturator lymph nodes via the dorsal vein of the clitoris, thus by-passing the usual lymphatic drainage of the vulva to the groin lymph nodes [4].

In this series, the most common stage at the time of diagnosis was Stage I (40% of the patients). A surgical staging system for vulvar carcinoma, which includes a well-defined set of surgicopathologic risk factors, was adopted by FIGO in 1988 and replaced the old FIGO clinical staging system for vulvar carcinoma [4,5]. Contrary to the old FIGO clinical staging system, the new FIGO surgical staging system for vulvar carcinoma defines the true extent of the disease and correlates better with clinical outcome. We have demonstrated with use of univariate and multivariate analysis that stage of disease is one of the most sensitive predictors of survival.

Patients accrual in this series occurred over a prolonged period of time during which treatment approaches and modalities changed. Most of the patients with vulvar squamous cell carcinoma (84%) presented in this report underwent surgery. The most prevailing type of surgery was radical vulvectomy and bilateral groin lymphadenectomy, which has been established as the mainstay of treatment in invasive vulvar carcinoma [4]. The role of radiotherapy in the management of vulvar carcinoma has been controversial [17]. In a variety of circumstances, it may be used preoperatively in order to reduce the size of the tumor, or it may be used as primary treatment, or it may be used as postoperative adjuvant therapy [4]. The use of chemotherapy in vulvar squamous cell carcinoma is experimental [4,18].

We, like others [19], have shown that the overall incidence of groin lymph node metastases in vulvar squamous cell carcinoma is ~30%. Like others [12,17,19], we have noticed that clinical palpation is not very reliable in detecting groin lymph node metastases. Overdiagnosis (clinically suspicious lymph nodes but negative pathologically, i.e., false positive) was present in five (55.5%) of nine patients. Underdiagnosis (clinically not suspicious lymph nodes but positive pathologically, i.e., false negative) was seen in three (27.3%) of 11 patients. In a previous study of 28 patients with vulvar malignancy, the data of which are included in the present report, we have found a false positive rate of 50% among the patients with clinically suspicious groin lymph nodes and a false negative rate of 8.3% among the patients with clinically not suspicious groin lymph nodes [20]. Iverson [21] in a study of 258 patients found a false positive rate of 15% among the patients with clinically suspicious groin lymph nodes. Way and Benedet [22] compared clinical palpation with histology of groin lymph nodes and found that 25% of histologically involved lymph nodes were clinically not suspicious, and 24% of histologically negative nodes were clinically suspicious. Plentl and Friedman [23] showed a 39% error in histologically positive nodes and a 35% error in histologically negative nodes. Since nonpalpable groin lymph nodes may contain cancer (false negative), modifications of surgical technique according to clinical assessment of groin lymph nodes is dangerous and radical vulvectomy and bilateral groin node dissection should be carried out on all these occasions. In contradistinction to other studies [24–27] that demonstrated that groin lymph node status is one of the most important prognostic factors, we could not demonstrate that groin lymph node status was a significant predictor of survival.

We have observed that in our series almost one-half of the patients who had radical vulvectomy had postoperative complications. This is in accord with the finding of Way [12] that 48.8% of his patients had postoperative complications. The postoperative complications most frequently encountered in this series was wound separa-

tion (26.7%) and and leg lymphedema (26.7%). In Way's series [12], wound breakdown occurred in 10% of the patients and various degrees of lymphedema (from trivial to gross) occurred in 65% of the patients.

We, like others [2,12,28], have observed that recurrent disease occurred in about one-third of the patients and that the vulva was the most encountered site affected by recurrence.

The actuarial 5-year survival in the present series was 60.3% and 78.2% for all stages and for Stage I only, respectively. These figures are significantly lower than the figures of 75% and 90% for all stages and for Stage I only, respectively, which have been reported in most textbooks [4,12,29]. The actuarial 5-year survival for Stage II (83.3%) in the present series was higher than that for Stage I (78.2%), but the difference was not statistically significant. The relatively low survival rate of the patients in the present series may be explained by one or more of the following reasons: (1) smallness of the series, (2) very long duration of the study period, and (3) delay in seeking medical assistance.

By means of univariate analysis, a significant worsening in survival has been demonstrated with advancing stage of disease ($P < 0.001$) and growing of the tumor beyond 4 cm in largest diameter ($P < 0.001$). Univariate analysis failed to demonstrate that each of the following variables, tumor site on the vulva, ethnic origin, age of the patient, tumor grade, and recurrence-free interval, was a significant predictor of survival. In patients who had surgery, by means of univariate analysis a significant worsening in survival has also been demonstrated with positivity of surgical margins ($P < 0.0001$). In a multivariate analysis of the following variables, stage of disease, tumor site on the vulva, tumor size, ethnic origin, and age of the patient in a group of 45 patients, stage of disease was the strongest and the only significant predictor of survival ($P = 0.0098$). However, in a multivariate analysis of the following variables, stage of disease, ethnic origin, tumor site on the vulva, age of the patient, tumor grade and status of surgical margins in a group of 34 patients who had surgery, status of surgical margins turned out to be a significant predictor of survival ($P = 0.0032$), whereas ethnic origin was of borderline significance ($P = 0.0484$).

In conclusion, vulvar squamous cell carcinoma is an uncommon malignancy that predominantly affects elderly women. Most distressing is the delay in diagnosis. Clinical palpation is not very reliable in detecting groin lymph node metastases, and omitting groin dissection because of clinically nonpalpable groin lymph nodes is dangerous. For most cases of vulvar squamous cell carcinoma, the treatment of choice is radical vulvectomy and bilateral groin lymphadenectomy. In a univariate analysis, each of the following variables, stage of disease, tumor size, and status of surgical margins, was a significant predictor of survival. In a multivariate analysis, stage of disease was the strongest and the only significant predictor of survival. However, in a multivariate analysis in a smaller group of surgically treated patients, status of surgical margins turned out to be the strongest significant predictor of survival.

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